بسم الله الرحمن الرحيم

عنوان المحاضرة: Carcinoma Of The Prostate
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Incidence & Epidemiology:

-Prostate cancer (CaP) is the leading cancer diagnosed and the second most common cause of cancer-related death in men in the United States (After lung cancer).

-Scandinavian countries have a particularly high rate of prostate cancer diagnosis and death compared with southern European countries.

-Life time risk for latent CaP of a 50-year old man is 40%

●Less than 40 ys.→1 : 10000 ●40-60 ys.→ 1 : 100 ●60-80 ys.→ 1 : 8

-Of all cancers, the prevalence of CaP increases the most rapidly with age.

-The incidence of CaP continues to increase with advancing age.

Risk Factors:

1-Increasing age heightens the risk of CaP

2-African American at a higher risk for CaP than whites
In addition, African American men tend to present in a later stage of the disease than whites

3-A positive family history of CaP

4-High dietary fat intake

5-Exposure to cadmium, which is found in cigarette smoke, alkaline batteries and in welding industry

6-Previous vasectomy has been suggested as a factor.

7-Antioxidants: Lycopene, selenium and vitamin E are associated with low risk for CaP

8-Risk of CaP is inversely proportional to sun exposure (increase in vit. D)

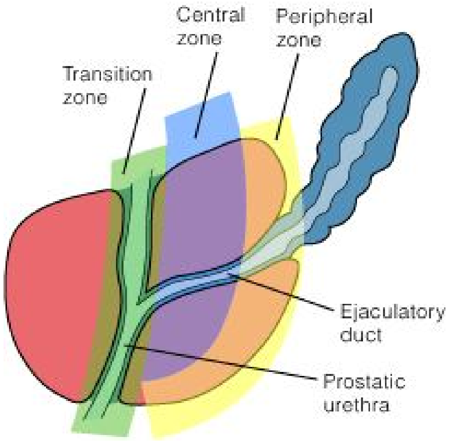
Pathology:

According to the zonal anatomy of the prostate: (By McNeal)

-70% of cases of CaP originate in the peripheral zones.

-20% originate from transition zone.

-10% originate from central zone.



-95% of CaP are adenocarcinoma.
The other 5% are transitional cell carcinoma. (Ductal carcinoma)

-The cytological characteristic of CaP include:

●Hyperchromatic enlarged nuclei with prominent nucleoli.

●Cytoplasm is abundant.

●Cytoplasm is often blue-tinged or basophilic. ●The basal cell layer is absent.

-Prostatic intraepithelial neoplasia (PIN):

-It is the precursor of invasive CaP.

-The critical distinguishing feature of invasive CaP is that the basal cell layer is absent.

-In PIN the basal cell layer is present

-PIN is classified into 2 categories: high grade and low grade

Grading and staging: (Gleason's Grading System)

It relies upon the low-power appearance of the glandular architecture.

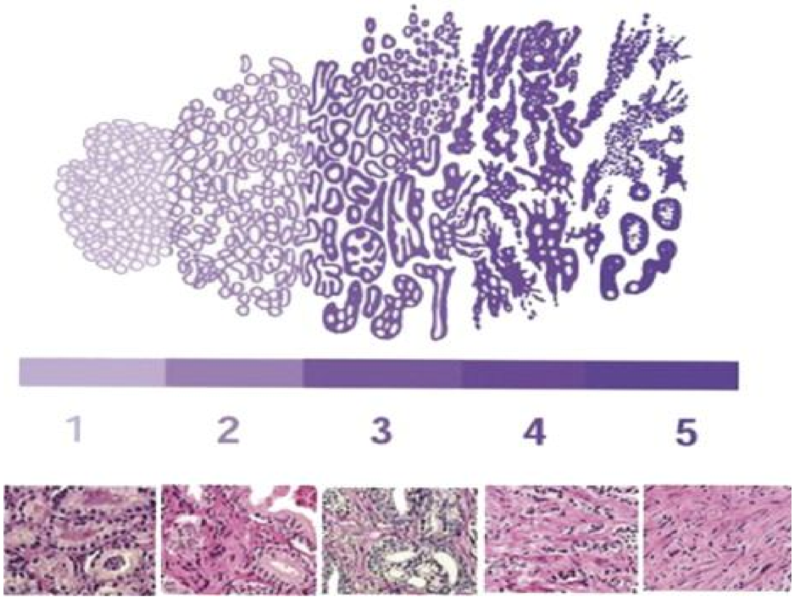
Grade 1 & 2: Small uniformly shaped glands closely packed with little intervening stroma.

Grade 3: Variable sized glands that percolate between normal stroma

Grade 4: Incomplete gland formation

Grade 5: No glandular differentiation and is composed of solid sheets, single cells, or solid nests of tumor

Primary grade: the predominant pattern.
2ry grade: the second most prevalent pattern



Gleason score (Sum):

By adding primary and secondary grades
2-4 → Well differentiated
5-7 → Moderately differentiated
8-10 → Poorly differentiated

TNM staging system

T: Primary tumor

- **Tx:** Primary tumor cannot be assessed
- **To:** No evidence of primary
- **T1:** Clinically unapparent tumor, not palpable or visible by imaging
  - **T1a:** incidental histological finding after TUR; in 5% or less of tissue resected.
  - **T1b:** incidental histological finding after TUR (Transurethral resection) ; in >5% of tissue resected.
  - **T1c:** Tumor identified by prostate needle biopsy because of elevated PSA.
- **T2:** Palpable tumor confined within the prostate (by DRE)
  - **T2a:** Tumor involves half of a lobe or less
  - **T2b:** Tumor involves >half of a lobe, but not both lobes
  - **T2c:** Tumor involves both lobes
- **T3:** Tumor extends through the prostatic capsule and/or involving seminal vesicles
  - **T3a:** Unilateral extracapsular extension
  - **T3b:** Bilateral extracapsular extension
  - **T3c:** Tumor invades seminal vesicle(s)
- **T4:** Tumor is fixed or invades adjacent structures other than semina vesicles
  - **T4a:** Tumor invades bladder neck &/or external sphincter &/or rectum
  - **T4b:** Tumor invades levator ms. &/or is fixed to the pelvic wall

N: regional lymph nodes

- **Nx:** regional lymph nodes cannot be assessed
- **No:** No regional lymph nodes metastasis
- **N1:** regional lymph nodes metastasis

M: Distant metastasis

- **Mx:** Distant metastasis cannot be assessed
- **Mo:** No Distant metastasis
- **M1:** Distant metastasis
  - **M1a:** Non regional lymph nodes metastasis
  - **M1b:** Bone metastasis
  - **M1c:** other sit(s)

Pattern of progression:

Local spread:

-The likelihood of local extension outside the prostate (extracapsular extension) or seminal vesicle invasion and distant metastases increase with increasing tumor volume and poorly differentiated cells

-Penetration of the prostatic capsule by cancer is common.

-Seminal vesicle invasion is often associated with **distant metastases.**

-Locally advanced CaP may invade bladder trigone and cause bilateral ureteral obstruction.

Distant metastases:

Lymph:

-Lymphatic metastases are most common identified in obturator, internal and external iliac and presacral lymph node chains (*same regional LNs of the Bladder*).

-Other sites of juxtaregional nodal metastases are common iliac, and periaortic lymph node.

Bone:
-The axial skeleton is the most common site of distant metastases.
-Lumber spine is the most common site.
-The lesion is almost **osteoblastic** in nature (↑ Bone density).
Soft tissue: Liver, lung, adrenal and brain.

Clinical finding:

A) Symptoms:

1-Most patients are asymptomatic.
2-Obstructive or irritative voiding symptoms can results from local growth of the tumor in the urethra or the bladder neck. (**BPH may accompany CaP but it isn't a precursor of malignancy**)
3-Metastatic disease to the bone can cause bone pain.
4-Metastases to the spinal cord can cause symptoms of cord compression.

B) Signs:

1-Physical examination can detect signs of distant metastases to bone.
2-**DRE examination**, we can palpate hard nodule, inequality of both lobes or hard prostate.
3-Sign of cord compression can be detected as weakness or spasticity in the lower limb.

D.D. of a hard nodule in the prostate: **(Last Year Exam)**
1-Prostatic carcinoma 2-Chronic Prostatitis 3-Calcular Prostatitis 4-TURP and needle biopsy

C) Laboratory finding:

1- Anemia can result from metastatic disease 2- ALP elevated in bone metastases

D) Tumor marker: Prostate Specefic Antegin (PSA)

-It is the most popular tumor marker for the prostate.
-It has great help with DRE and TRUS for detection of CaP.
-PSA is not specific to the prostate cancer so we can say it is **organ specific** not tumor specific.
-PSA can be elevated in:
Uretheral instrumentation, BPH, infection, ejaculation, urine retention and vigorous DRE
-Normal value less than 2.6 ng/dl
-PSA range 2.6 - 10 ng/dl. **Lakes specificity**
**** To improve specificity**
-*PSA density:* (PSA/ prostate volume) ● > 0.15 is the proposed threshold to perform biopsy
-*PSA velocity:* (Change of PSA / change of time) ● A rise > 0.75 ng /ml in a year is cause for concern.
-*Free PSA:* Patients with prostate cancer tend to have lower **free** / **total** PSA ratio.
Ratio of 25% has proposed as cut-off value.

E) Prostatic biopsy:

1-Systematic sextant prostatic biopsy is the most commonly employed technique in detection of CaP
2-Biopsies are usually obtained under TRUS guidance

F) Imaging:

1- TRUS
2- Other methods of imaging:
-Endorectal magnetic resonance imaging -Axial imaging (CT, MRI),(lymph node metastasis)
-Bone scan (high PSA, High Grade)

Treatment:

A-Watchful waiting (deferred treatment):

- Localized cancer **T1a –T2c** with **short life expectancy** (< 10 yrs) and well diff. tumors (Gleason score 2-4)
- **Patients** not willing to accept the side effects of **active treatment.**
- Well informed asymptomatic patient with high PSA levels for whom cure is unlikely.
- T3, T4 Asymptomatic patients with Gleason score 6 or less with short life expectancy.

B-Active Treatment:

1- In localized cases (organ confined):

- T1a: life expectancy more than 15 years (optional)
- T1b-T2c: life expectancy more than10 years

A-Radical prostatectomy: It has 2 types: perineal or retropubic.

Retropubic prostatectomy: open, laparoscopy

In this operation we remove:

(The whole prostate - Both seminal vesicle - Vas deferens - The prostatic urethera - Lymph nodes)

Complication of radical prostatectomy: (Bleeding - Rectal injury - Ureteral injury - Deep venous thrombosis - Lymphocele formation - Urinary incontinence - Impotence)

B-Cryosurgery:

Freezing of the prostate is carried out by using a multiprobe cryosurgical device.

It is used under TRUS guidance.

It is useful in selected localized cases.

C-Radiotherapy and Brachytherapy

2- In Locally advanced cases:

A-Radical prostatectomy

T3a: PSA < 20 ng/ml, Gleason score < 7 with life expectancy >10 years

B-Radiation therapy- external beam therapy.

C-Brachytherapy: (Radioactive seeds under TRUS guidance)

3- In Metastatic cases:

A- Hormonal therapy:

As the CaP is hormonal dependant tumor, the use of hormonal therapy may be useful.

►If Hormonal Dependent: It is carried out by androgen deprivation therapy.

It can be done by: (Bilateral orchiectomy - Diethylstilbesterol - LHRH analogue - Antiandrogen)

B- In case of hormonal refractory cases: Chemotherapy